

## AMENDMENTS TO THE DRAWINGS

The attached Replacement Sheet of drawings includes changes to Figures 7A-7E. This Replacement Sheet corrects the Figure identifier to recite Figures 11A-11E because two different sheets having a Figure 7 identifier were inadvertently submitted as formal drawings. The Replacement Sheet replaces Figures 7A-7E (sheet 9) as originally filed.

Attachment: Replacement Sheet  
Annotated Marked-Up Drawing Sheet

## REMARKS

### **I. Status of the Application**

Claims 1-24 are presently pending in the application. Claims 2-9, 11-13 and 22 have been cancelled without prejudice to the filing of any appropriate continuation applications. Claims 1-24 stand provisionally rejected under 35 U.S.C. §101 as being anticipated by copending Application No. 10/008,456. Claims 1-18 stand provisionally rejected under the judicially created doctrine of obviousness-type double patenting over copending Application No. 10/008,456 in view of Phelan et al. (1998) *Arch. Biochem. and Biophys.* 357:155. Claims 1-17 and 21-23 stand rejected under 35 U.S.C. §112, first paragraph, as lacking enablement. Claims 2 and 9 stand rejected under 35 U.S.C. §112, second paragraph, as indefinite. Claims 1, 10, 14, 18, 19, 21, 23 and 24 stand rejected under 35 U.S.C. §102(b) as being anticipated by Rhine et al. (1999) *J. Perinatol.* 19:206. Claims 1-3, 6, 10, 14 and 18-24 stand rejected under 35 U.S.C. §102(b) as being anticipated by Notter et al. (1986) *Exp. Neurol.* 94:670. Claims 18, 19 and 24 stand rejected under 35 U.S.C. §102(b) as being anticipated by Sima et al. (1980) *Folia Microbiologica* 25:483. Claims 7-9 and 15-17 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Rhine et al. or Notter et al.

Applicant gratefully acknowledges the Examiner's indication that the promotion of differentiation in colon adenocarcinoma cells is allowable subject matter. In response, Applicant has amended the pending claims to recite methods for promoting cell differentiation in colon adenocarcinoma cells.

Support for the amendments to the specification can be found in the Brief Description of the Drawings at page 5 of U.S. Provisional Application 60/128,653, filed April 8, 1999. The

Brief Description of the Drawings was incorporated by reference in its entirety in the instant application.

Support for the claim amendments can be found throughout the specification and claims as originally filed. Specifically, support for promoting cell differentiation can be found in claim 11 as originally filed which recites “promotes cell differentiation,” and in the specification at least at page 1, line 25, where Applicant teaches promoting cell differentiation. Support for colon adenocarcinoma can be found in the specification at least at page 63, lines 1-15, where Applicant teaches the induction of differentiation in colon adenocarcinoma (i.e., HT29) cells. Support for the amendments to claim 17 to recite regulation of pancreas, small intestine and spleen can be found at least at page 28, fourth full paragraph and page 29, first full paragraph, where Applicant teaches “generation the of pancreas and small intestine from the embryonic gut” and “controlling the development and maintenance of tissue from the digestive tract, spleen, lungs, and other organs which derive from the primitive gut.” The amendments presented herein add no new matter.

Applicant respectfully requests entry and consideration of the foregoing amendments, which are intended to place this case in condition for allowance.

## **II. Claim Objections**

At page 3, paragraph 1 of the instant Office Action, the Examiner objects to the disclosure for failing to provide a brief description of each drawing. In response, Applicant has amended the specification to provide a brief description of the drawings. Accordingly, Applicant respectfully requests that this objection be withdrawn.

### **III. Double Patenting Rejections**

At page 4, paragraph 3 of the instant Office Action, claims 1-24 stand provisionally rejected under 35 U.S.C. §101 as claiming the same invention as that of claims 1-17, 19-20 and 23-25 of copending Application No. 10/008,456. At page 4, paragraph 7 of the instant Office Action, claims 1-18 stand provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 27-43 of copending Application No. 10/008,456.

Applicant respectfully traverses these rejections in view of the amended claims presented herein. As amended, the instant claims are directed to methods of, and pharmaceutical preparations for, promoting differentiation of colon adenocarcinoma cells. In contrast, the pending claims in copending Application No. 10/008,456 will be amended such that they are directed to methods of promoting cell differentiation in a cell selected from the group consisting of liposarcoma cell, thyroid carcinoma cell and lymphoblast cell. Thus, the pending claims are distinct in scope from the pending claims of the '456 Application. Accordingly, Applicant respectfully requests that these rejections be reconsidered and withdrawn.

### **IV. The Pending Claims Are Enabled**

At page 6, paragraph 2 of the instant Office Action, claims 1-9, 21 and 22 stand rejected under 35 U.S.C. §112, first paragraph as lacking enablement. The Examiner is of the opinion that the specification, while being enabling for inhibition of cell proliferation, does not reasonably provide enablement for promoting cell proliferation. Applicant respectfully traverses this rejection.

Without acquiescing to these rejections, Applicant submits that claims 2-9 and 22 have been cancelled without prejudice to the filing of any appropriate continuation applications to facilitate allowance of the case. As amended, claims 1 and 21 recite a method of promoting colon adenocarcinoma cell differentiation. Claims 1 and 21 do not recite promoting cell proliferation. Accordingly, Applicant respectfully requests that this rejection be reconsidered and withdrawn.

At page 7, paragraph 2 of the instant Office Action, claims 3-4, 11 and 12 stand rejected and at page 8, paragraph 2 of the instant Office Action, claims 5 and 13 stand rejected under 35 U.S.C. §112, first paragraph as lacking enablement. The Examiner is of the opinion that the specification does not reasonably provide enablement for inhibition or promotion of cell proliferation or differentiation at concentrations of 1 mM or less, 1  $\mu$ M or less or 1 nM or less.

Applicant traverses these rejections and respectfully submits that the specification enables the claimed concentrations. Without acquiescing to these rejections, Applicant submits that in order to facilitate allowance of the case, claims 3-5 and 11-13 have been cancelled without prejudice to the filing of any appropriate continuation applications, thus rendering these rejections moot.

At page 9, paragraph 2 of the instant Office Action, claims 1, 10-17, 21 and 23 stand rejected under 35 U.S.C. §112, first paragraph as lacking enablement. The Examiner is of the opinion that the specification, while being enabling for promoting differentiation in colon adenocarcinoma cells, does not reasonably provide enablement for promotion of differentiation in any other type of cell.

Applicant traverses this rejection. Without acquiescing to the rejection, Applicant submits that the pending claims have been amended to recite promoting differentiation in colon

adenocarcinoma cells in order to facilitate allowance of the case. As the Examiner has indicated that promoting cell differentiation in colon adenocarcinoma is enabled, Applicant respectfully requests that this rejection be reconsidered and withdrawn.

**V. The Pending Claims Are Definite**

At page 11, paragraph 1 of the instant Office Action, claims 9 and 17 stand rejected under 35 U.S.C. §112, first paragraph as being indefinite. The Examiner is of the opinion that the metes and bounds of the phrases “other organs arising from the primitive gut” and “etc” are unclear.

Without acquiescing to the rejection, Applicant respectfully submits that claim 9 has been cancelled without prejudice to the filing of any appropriate continuation applications to facilitate allowance of the case. Claim 17 has been amended to replace the language “and other organs arising from the primitive gut” with specific organs that arise from the gut. The term “etc.” has been deleted. Applicant respectfully submits that claim 17 is definite and accordingly requests that this rejection be reconsidered and withdrawn.

**VI. The Pending Claims Are Novel And Nonobvious Over the Cited Art**

Claims 1, 10, 14, 18, 19, 21, 23 and 24 stand rejected under 35 U.S.C. §102(b) as being anticipated by Rhine et al. (1999) *J. Perinatol.* 19:206. Claims 1-3, 6, 10, 14 and 18-24 stand rejected under 35 U.S.C. §102(b) as being anticipated by Notter et al. (1986) *Exp. Neurol.* 94:670. Claims 18, 19 and 24 stand rejected under 35 U.S.C. §102(b) as being anticipated by Sima et al. (1980) *Folia Microbiologica* 25:483. Claims 7-9 and 15-17 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Rhine et al. or Notter et al.

At page 14 of the instant Office Action, the Examiner indicates that “[t]he promotion of differentiation in colon adenocarcinoma cells by a claimed bilin appears to be neither anticipated nor obvious over the prior art” and is allowable subject matter.

While Applicant respectfully traverses the Examiner’s rejections of the claims as being anticipated by Rhine et al., Notter et al or Sima et al., and as being obvious over Rhine et al. or Notter et al., Applicant has amended the claims to recite methods and pharmaceutical formulations for promoting colon adenocarcinoma cell differentiation by a bilin in accordance with the Examiner’s indication of allowable subject matter. Accordingly, Applicant respectfully requests that these rejections be reconsidered and withdrawn.

## **VII. Conclusion**

Having addressed all outstanding issues, Applicant respectfully requests entry and consideration of the foregoing amendments and reconsideration and allowance of the case. To the extent the Examiner believes that it would facilitate allowance of the case, the Examiner is requested to telephone the undersigned at the number below.

Respectfully submitted,

Dated: April 5, 2004

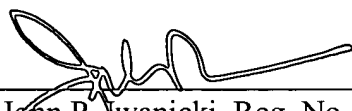
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FIG. 7A  
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FIG. 7B  
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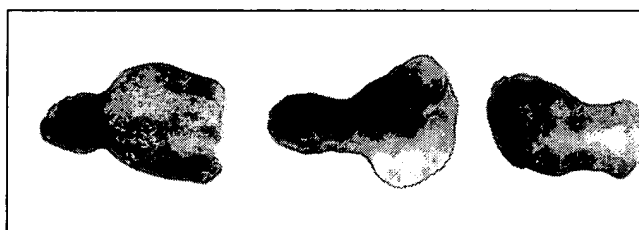


FIG. 7C  
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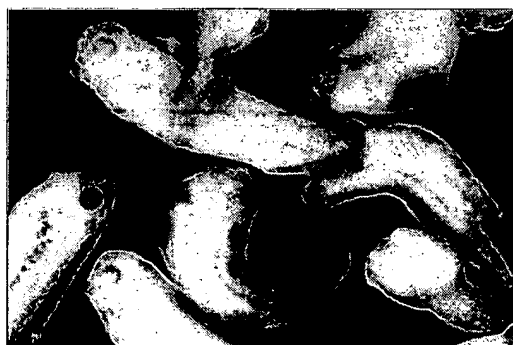


FIG. 7D  
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FIG. 7E  
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